REMARKS

The Examiner rejects claims 1, 6 to 11 and 26 to 31 based upon the written description requirement under 35 USC 112, first paragraph. The Examiner states that modified botulinum neurotoxin molecules have not been described and that the specification fails to describe what amino acids exactly comprise the structural modifications of the neurotoxin molecules. Applicant traverses this rejection.

The specification describes structural modifications of neurotoxins, including botulinum toxins, which alter biological persistences. For example, page 20, lines 4 to 22 of the specification and Example 9, starting on page 34 of the specification, disclose structural modifications wherein leucine-base motifs are fused to neurotoxins and structural modifications wherein neurotoxins are recombinantly produced with non-native leucine-based motifs. In addition, the specification discloses on page 20, line 24 to page 21, line 2, and in Example 10, starting on page 35, structural modifications of neurotoxins wherein one or more amino acids are deleted from a leucine-based motif which is native to the neurotoxin, for example, a botulinum toxin type A.

Examples of leucine-based motifs which can be added to a toxin, and their amino acid sequences, are disclosed, for example, in Table 1 on page 18 of the specification and in SEQ ID NOS: 1 to 18. An example of a leucine based motif from which one or more amino acids may be deleted is a leucine based motif of a botulinum toxin type A which is disclosed in the specification, for example, on page 17, lines 17 to 18 and in SEQ ID NO: 1.

Therefore, since the specification makes clear that leucine-based motif structural modifications of neurotoxins, including botulinum toxins such as botulinum toxin type A, are contemplated in the invention and discloses amino acid sequences which comprise certain leucine based-motifs sequences useful in

such neurotoxins, applicant submits that the present claims comply with the written description requirement.

The Examiner states that the pending claims meet the enablement requirement under 35 USC 112, first paragraph for specific botulinum toxins with a definable sequence change and a definable assayable function.

Applicant presents herein new claims 44 to 64 which comply with the Examiner's requirement for enablement. The new claims are directed to a specific botulinum toxin, i.e., botulinum toxin type A, with a definable sequence change, i.e., a leucine-based motif structural modification, and a definable assayable function, i.e., an altered biological persistence. Hence, applicant submits that the new claims are enabled.

The Examiner rejects the pending claims as being indefinite under 35 USC 112, second paragraph. The Examiner states that what constitutes a "modified neurotoxin" is ambiguous in that no "structural modifications" are recited in the claims. The Examiner rejects claim 7 as indefinite because, the Examiner states, the phrase "leucine-based motif without one or more amino acids" is confusing. The Examiner also rejects claims 10, 11 and 26 to 31 stating that the term "substantially derived" makes the claims ambiguous.

In response to this rejection, applicant has canceled the rejected claims. New claims which recite specific structural modifications have been added. In particular, the new claims recite the feature of "a leucine-based motif structural modification." In addition, the new claims do not refer to "leucine-based motif without one or more amino acids." Also, the term "substantially derived" is not included in the new claims.

In view of the above, applicant submits that claims 44 to 64 satisfy the requirements of 35 USC 112, second paragraph, and respectfully request that the rejection based on this statutory provision be withdrawn.

The Examiner rejects claims 1, 6 to 11 and 26 to 31 under 35 USC 102(b) citing U.S. Patent No. 5,939,070 (Johnson et al).

Applicant traverses this rejection as it pertains to claims 44 to 64.

Johnson et al does not disclose, teach or even suggest the present invention which relates to neurotoxins, for example, botulinum toxins, with structural modifications, for example, leucine-based motif structural modifications, which alter the biological persistence of the neurotoxins. For example, Johnson et al does not disclose, teach or even suggest that a modified toxin will have an altered, for example, a reduced, biological persistence. In addition, the present claims recite the feature of a leucine-based motif structural modification. Nowhere in Johnson et al is there any disclosure, teaching or suggestion relating to leucine-based motif structural modifications, as recited in the present claims.

In view of the above, applicant submits that claims 44 to 64 are not anticipated by, and are unobvious from and patentable over, Johnson et al under 35 USC 102(b) and 103.

In conclusion, applicant has shown that the present claims satisfy the requirements of 35 USC 112, and are not anticipated by, and are unobvious from and patentable over the prior art under 35 USC 102 and 103. Therefore, applicant submits that new claims 44 to 64 are allowable and respectfully requests the Examiner to pass the above-identified application to issuance at an early date.

When the Examiner allows the present claims, applicant respectfully requests the Examiner to consider allowing claims relating to the non-elected species of botulinum toxin serotypes B, C, D, E, F, and G. Since all botulinum toxins are believed to operate by a similar mechanism of action, the search performed for botulinum toxin type A should suffice for all of the botulinum toxin serotypes. For example, it is well known that "The botulinum toxins comprise a family of pharmacologically similar toxins that block acetylcholine release from peripheral nerves and cause flaccid paralysis. All of the serotypes of the toxin can poison humans and other

animals...", Page 81, left hand side of Schantz, E.J., et al, *Properties and use of Botulinum Toxin and Other Microbial Neurotoxins in Medicine*, Microbiol Rev., 56;80-99:1992 (copy provided with response to Office Action mailed September 27, 2002).

Respectfully submitted,

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